

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:  
James Berger Camden et al.

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(in parent appl'n: P. Spivack)

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(in parent appl'n: 1614)

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For: Viral Treatment

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Commissioner of Patents  
Washington, D.C. 20231

Sir:

**PRELIMINARY AMENDMENT**

This Preliminary Amendment is being filed concurrently with a Request to File a Divisional Application. Please amend the application as indicated below.

**AMENDMENT**

Attached is a marked-up version of amended specification paragraphs and amended claims where language deleted is in brackets, and language added is underlined.

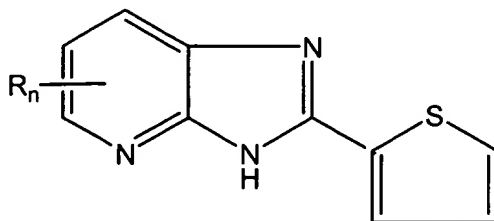
**In the Specification:**

The priority paragraph at page 1, line 8 has been rewritten to read:

The present application is a divisional application of USSN 09/538,006 filed March 29, 2000, *now* from which priority under 35 U.S.C. §120 is claimed. USSN 09/538,006 is a continuation in part of application of J.B. Camden, serial number 09/281,892, filed March 31, 1999, *abandoned*.

The paragraph beginning on page 3, line 22, is amended to read:

A pharmaceutical composition for treatment of viral infections in patients in need thereof, and in particular, warm blooded animals and humans, comprising a pharmaceutical carrier and an effective amount of an anti-viral compound having the formula:



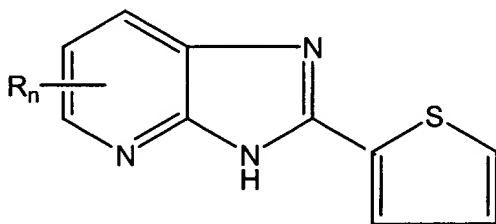
A2 wherein n is 1 to 3; and R is selected from the group consisting of hydrogen, alkyl having from 1 to 7 carbon atoms, chloro, bromo, fluoro, oxychloro, hydroxy, sulfhydryl, and alkoxy having the formula  $-O(CH_2)_yCH_3$  wherein y is from 0 to 6, its prodrugs and pharmaceutically acceptable salts.

The paragraph beginning on page 4, line 12, is amended to read:

A3 These materials are active against *Cryptococcus neoformans* and *Curvularia lunata*. Both of these are fungi which are found in AIDS patients.

The paragraph beginning on page 5, line 23, is amended to read:

As used herein, the "thienyl imidazolo[4,5]pyridine derivatives" or "2-thienyl imidazolo[4,5]pyridine compounds" or "2-(2-thienyl)imidazolo[4,5-b]pyridine compounds" are the members of the group of compounds having the formula:



wherein n is 1-3; and R is selected from the group consisting of hydrogen, alkyl having from 1 to 7 carbon atoms, chloro, bromo, fluoro, oxychloro, hydroxy, sulfhydryl, and alkoxy having the formula  $-O(CH_2)_yCH_3$  wherein y is from 0 to 6, its prodrugs and pharmaceutically acceptable salts.

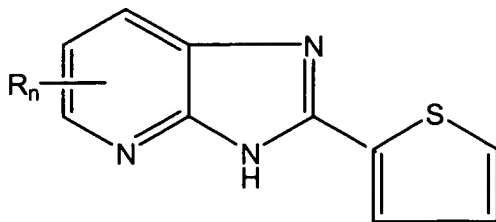
The paragraph beginning at page 6, line 28, is amended to read:

A5 As used herein "viruses" includes viruses which infect animals or mammals, including humans. Viruses include retroviruses, HIV, influenza, polio viruses, herpes simplex, hepatitis B, hepatitis C, other hepatitis viruses, Kaposi's sarcoma virus, rhinoviruses, bovine diarrhea virus, and the like. HIV and AIDS are immunosuppressant diseases.

The paragraph beginning at page 7, line 7, is amended to read:

The 2-thienyl imidazolo[4,5]pyridine compounds useful herein have the formula:

A6



wherein n is 1-3; and R is selected from the group consisting of hydrogen, alkyl having from 1 to 7 carbon atoms, chloro, bromo, fluoro, oxychloro, hydroxy, sulfhydryl, and alkoxy having the formula  $-O(CH_2)_yCH_3$ , wherein y is from 0 to 6, preferably from 1 to 6. Preferably the 2-thienyl imidazo[4,5]pyridine is substituted with an alkyl of less than 4 carbons, a halogen (preferably a chloro), nitro, hydroxy or oxychloro in the 7 or 8 position and the remaining substituents of the pyridine ring are hydrogen.

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The paragraph beginning at page 32, line 24, is amended to read:

2-(2-thienyl)imidazo[4,5-b]pyridine was tested against Kaposi's Sarcoma, a herpes virus, in vitro using the Human Herpes Virus 8 (HHV8) cell line, TPA-induced BCBL-1 cells. The DNA copy number and the toxicity value were measured and compared with Cidofovir. Kaposi's sarcoma (KS) is a cancer that is often found in people with weak immune systems, such as those taking immunosuppressants or those with AIDS. The exact nature of the disease is uncertain, but it is almost always found in association with HHV8. Recent studies suggest that KS is caused by the herpes virus; that is, that KS is a herpes virus that manifests itself as a cancer.

The paragraph beginning at page 34, line 3, is amended to read:

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2-(2-thienyl)imidazo[4,5-b]pyridine was tested against a number of fungi *in vitro*. It was active against *Cryptococcus neoformans* and *Curvularia lunata*. The cidal activity for the *C. neoformans* is high enough that it is clear static against this yeast. This test was conducted using a method based upon NCCLS reference method M-27A published in 1997. Solvent, medium and growth controls were set-up with the tests. Once these were read to validate the test performance, the QC fungi were read to insure they had expected results. These steps validated the test system. DMSO was used as a drug-chemical solvent. These tests were read following incubation at 35°C when the QC organisms (*Candida* spp.) showed good growth. MIC values were concentrations in which growth was inhibited or reduced at least 90% in comparison to the control growth. The 90% cut-off is necessary for azoles, which are static and not cidal. The FMC or cidal level was determined by sub-culturing a sample from each tube showing no growth.